

MYRIAD GENETICS

Executing the Vision of Molecular Medicine

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In the next 20 years, the ways people manage their health will change radically. You will still go to see a doctor for antibiotics or medications to treat infectious diseases, and for emergencies such as trauma resulting from accidents. But for many degenerative disorders and conditions that take years to develop--including cancer, diabetes, heart disease, Alzheimer's, multiple sclerosis, hypertension, and high cholesterol--the eventuality of onset, and the means to treat or prevent that onset, will have been determined years in advance.

In the next few years, you will be administered a battery of genetic predisposition tests that will portray a picture of your future health as clearly as a photograph. Teams of scientists and doctors will work together in a revolutionary new field called molecular medicine. Rather than being confronted and shocked with this "bad news," however, many of us who discover what is in store in our future will be able to smile and hope, because diseases that used to be inevitable will now be cured before they ever occur.

Once the predisposition for a disease has been established, that same team of doctors and researchers will prepare a completely individualized course of treatment involving lifestyle changes and medications that turn appropriate genes on and off, to preserve health and normal cellular molecular function before that machinery can malfunction.

Obviously, it would do little good to diagnose a molecular defect if there were no way to treat it, and there would be no way to develop the necessary drugs if we didn't know who to give them to. In addition, if you didn't know how the molecular machinery worked, you could neither test nor treat patients. It might seem like a daunting task to coordinate all three of these objectives, but Salt Lake City-based Myriad Genetics Inc. is doing exactly that.

Myriad is noteworthy in a number of ways. In addition to simultaneously advancing molecular medicine on three separate fronts, the company is located in Utah, hundreds or thousands of miles away from the biotechnology corridors around the country where many assume the critical mass of brainpower and resources necessary to be effective as a global pharmaceutical concern are located.

Myriad has also been remarkably successful in forming strategic alliances for research and commercial development of their discoveries, with companies including Schering, Lilly, Bayer, Novartis, Pharmacia, and Roche (with an estimated value of \$414 million in milestone and future royalty payments).

At the same time, Myriad is training and deploying a global sales force to sell its products and services directly.

The business and research communities have endorsed and validated the company's approach to molecular medicine, as evidenced by a strong record of publications in the scientific literature, over 450 employees, and a market valuation that now exceeds \$1 billion.

A BIT OF BACKGROUND

Myriad has been heavily involved in study of the human genome, i.e. the genetic material (DNA) inside every cell that provides the instructions for how to make a person or a frog or a bacterium. The DNA, when properly read, serves as the blueprint to make the structures of a body. A gene is a specific stretch of DNA responsible for a particular function; only about 5 percent of the DNA comprises actual functional genes.

In the past few years, the entire sequence of the human genome has been sequenced; that is, we know the structure of the DNA. However, we have only begun to identify which 5 percent are actual genes; current estimates predict that humans have between 30,000 and 45,000 genes.

Genes themselves can be turned on or off; when activated, they supply the instructions to make proteins, the actual structure and functional machinery of the body. Proteins make up the cells and tissues of the body, and also provide the enzymes and other substances that control and carry out all of the biological functions in a body. The collection of all proteins in the body is referred to as the proteome, and the study of the function of the proteins encoded by genes is called proteomics.

Armed with this background, it becomes apparent that knowing the sequence of the DNA does little good if one doesn't know where the genes are, what proteins they make, and how the production of those proteins can be turned on and off. It is generally accepted today that virtually all disease is caused or can be affected by abnormal protein function and interaction. Thus, genomics is in decline as an applied medical science relative to the hot new field of proteomics.

Proteomics has the potential to uncover the biological mechanisms underlying all disease, and Myriad Genetics has positioned its research and drug development efforts at the confluence of gene regulation, protein production, and protein interaction studies. The company's rationale is that by understanding how these areas are related, it will be possible to identify those critical points in a disease process at which a drug would be most effective in blocking excessive protein function, or activating deficient protein production.

Because there are so many genes, it is likely that the targets Myriad identifies for drug development will be highly specific for a particular molecular defect or disease--meaning that these drugs should be highly specific and free of side effects. This has important significance from a business standpoint, because the longest and most expensive part of drug development is the clinical trials, where side effects are identified and drug candidates are eliminated if they are toxic. At present only one in 10,000 compounds ever goes from discovery into a human; Myriad has good reason to expect it can significantly improve this batting average.

A UNIQUE CORPORATE STRUCTURE

Myriad Genetics is organized into functional units that complement one another, while focusing on each of the pillars of molecular medicine. Myriad Genetic Laboratories Inc.

develops the diagnostic tests that allow physicians to determine pre-dispositions to disease. Myriad Pharmaceuticals Inc. searches for and develops treatments for these conditions. Myriad Proteomics Inc. (a newly-formed joint venture between Myriad, Oracle and Hitachi, 50 percent owned by Myriad) intends to discover every protein encoded by every gene in the body and create a map of the human proteome. This information will be supplied to the other divisions.

In addition, Myriad Genetics has centralized the research labs and intellectual property protection operations to serve all of the divisions, avoiding duplication of effort and resources.

Myriad Genetics CEO Peter Meldrum explains why this corporate structure is so effective: 'The pharmaceutical business is very different than the diagnostics business; you have totally different skill sets and types of individual. Myriad has always been very entrepreneurial, and we want to encourage that.

"By setting up separate subsidiaries, not only can we attract people with the specific talents that we are looking for, but they are then responsible for the success of that subsidiary. It creates an entrepreneurial environment where they can make decisions and succeed and be rewarded for that success."

MOLECULAR DIAGNOSTICS: THE LEAD-OFF BATTER OF THE LINEUP

Myriad Genetic Labs Inc. was established as the original division of the company in 1991. It is the "predictive medicine" subsidiary that develops and markets diagnostic genetic tests for use by physicians. This division currently has available the BRACAnalysis panel for detection of predisposition to breast and ovarian cancers, COLARIS for the detection of nonpolyposis colorectal cancer and endometrial cancer risk, and Cardiarisk to detect salt-dependent hypertension.

In development are tests for melanoma predisposition (Melaris), prostate cancer (Prolaris), diabetes, and heart disease. This unit experienced 94 percent growth for fiscal year 2001, on earnings of \$17.1 million; this is estimated to exceed \$100 million by 2006. The worldwide market for the BRACAnalysis, COLARIS, and CardiaRisk tests is estimated to be around \$1.2 billion. With the tests now in development, that figure grows to \$2.1 billion.

The market acceptance of these tests is expected to accelerate with increased public acceptance of molecular diagnostic testing, and increased use of the tests by physicians. This will be aided by an alliance with Laboratory Corporation of America (LabCorp) to market the tests to 200,000 primary care physicians through LabCorp's 600-person U.S. sales force.

"In the US population about 1 in 700 have a deleterious mutation in a gene, leading to an elevated risk for breast cancer," says Dr. Gregory Critchfield, president of Myriad Genetic Labs. "Given these numbers, there are enough people in the US who carry it to equal the population of Cincinnati. It is a huge number of people. It is important to identify not only these people, but also their families, so they can do something about it.

"As we develop new tests, we have also been very involved in the education of doctors to teach them about genetics; this is a new paradigm, and a new approach to diagnosis. Managed care companies and insurance companies are very interested in preventing disease. What we are doing is giving very specific information on the genetics and the risk predictions that are important in helping someone prevent a future disease. We are really breaking new ground."

MYRIAD PHARMACEUTICALS: THE TALENTED ROOKIE

Myriad Pharmaceuticals Inc. is a toddler by comparison to the diagnostics division, but a savant by any standard. Since being founded in 1999, the division has identified 1,046 novel proteins and over 56 novel drug targets, resulting in 12 compounds put into the therapeutic pipeline.

Only one of these compounds came from outside the company. MPC- 7869 is currently in human clinical trials for treatment of colon and prostate cancer, and could be on the market by the end of 2004. A second compound, MPI -42511, is in preclinical trials for the treatment of colon cancer. Other compounds are in development for the treatment of cancers, AIDS, Hepatitis B, and rheumatoid arthritis.

This demonstrates the power of the corporate research and business strategy, because once a drug reaches the market, it will have synergistic benefit to the corresponding diagnostic test that indicates when it should be prescribed. This is a model that is not currently employed by any other pharmaceutical company.

Adrian Hobden, president of Myriad Pharmaceuticals (and a former 17-year veteran at Glaxo- Wellcome) explains their strategy: "We are competing with the large pharmaceutical companies. We have to do things quicker and smarter than they do. And we don't want to do anything that they are doing, because they are going to beat us. That really that means that we need to have a good way of identifying novel drug targets.

"Part of the reason I came to Myriad was that I saw they actually had a means to discover drug targets, using the ProNet technology (a proprietary yeast hybrid system for identifying novel proteins). Between this technology and the huge amount of automation built into the system, we have been able to screen compounds quickly and cheaply."

The pharmaceutical division is unique in other respects. The costs of clinical trials are enormous, which accounts for the fact that few pharmaceutical entities other than "big pharma" are able to single-handedly afford this expense. Thus, most small pharmaceutical and biotech companies form partnerships with the large companies to conduct trials, with the partners taking a royalty or ownership stake in the small partner.

Not so with Myriad. Because the company is already cash-flow positive in the molecular diagnostic testing market, the profits of that division will support the costs of clinical trials in the pharmaceutical division. The implications are enormous, because if and when a Myriad drug makes it to market, the company will be keeping the 40 percent or more of royalties that would otherwise go to the partner.

Another unique attribute of Myriad Pharmaceuticals is that the parent company formed the entity from scratch only two years ago. Most pharmaceutical companies are much older and are saddled with personnel, outdated or irrelevant equipment, and overhead left over from previous projects. Myriad has been able to build a division that is not only current but specifically configured for the research efforts of the company into the next several years. It can be thought of as a Porsche Boxter racing against that old Honda Accord.

CREATIVITY. WISDOM. SKILL. VISION.

The excitement surrounding Myriad Genetics in both the scientific and investment communities comes not just from the discoveries that have been made and the market potential, but also the willingness of the company to take calculated chances on new technologies, forge strong alliances, employ an integrated approach to both molecular disease detection and treatment, maintain a strong basic research effort, and define a field that is only coming into existence rather than waiting for others to define it.

"The genius of Myriad has been the creation of an integrated technology platform to study genomics, and now proteomics, in a way that other companies have not been able to do," says Critchfield.

Hobden adds: "Myriad Genetics is serious about creating a drug company in Utah. We don't have to be in New Jersey and the size of Merck to achieve it. It is possible to establish something from nothing and to grow it, through the right vision and the right insights, into a viable research and pharmaceutical company. We intend to still be here 10 years from now."

CEO Meldrum adds his own perspective: "We believe that the future of medicine is in understanding the actual causes of human disease and then developing drugs to treat those causes. Most of the drugs on the market today treat symptoms, not causes. We wait for a person to get sick and only then do we intervene and treat the disease. It is completely reactionary. Medicine over the next two to three decades will focus on preventing disease.

"Myriad Genetics recognizes the dawn of this paradigm shift, and we are well positioned to capitalize on it. Not only is it better for the patient, but it will also lower healthcare costs, because it is much cheaper to prevent disease than it is to treat a sick person."

THE FUTURE OF UTAH'S BIOTECH COMMUNITY

Much thought and discussion have been given to creating critical mass to launch a major economic initiative in the biotechnology sector in Utah. The resources, depth and breadth of talent, and success of Myriad Genetics can be seen as an anchor for building that community here.

Dr. Critchfield explains: "The research universities are producing excellent scientists; you have people who are bright and motivated at the University of Utah, which is well known for its pioneering work in the area of human genetics.

"This state needs to be committed to science education, getting kids to understand that they can have exciting, fulfilling, interesting careers in science. Growing a generation that is really interested in this area is both a challenge and a tremendous opportunity for Utah."

Hobden addresses the critical mass issue: "It is like setting up a shopping mall. If you just have one shop there, it won't do very well because people don't come to one shop. You need to get 10, and then everyone benefits. I think the good thing about Myriad now is that we have reached sufficient size that there are going to be job opportunities for people if they have the right skills.

"Myriad will get to the point soon enough that you will start to see spin-offs, and the logical place to put them is here. Then we will need to be able to accelerate beyond that point by attracting companies from other regions."

Meldrum adds: "I think Utah is very forward looking in assessing and supporting new business. Over the next decade, the greatest growth potential is in IT and biotechnology. The state has been a long-time supporter and encourager of both those industries. "Utah has the infrastructure to support a biotech industry. The research institutions in the state will not only support the biotech industry, but those new companies spun off of university research.

"I would like people to know and appreciate that in Utah we are doing world-class research. We are making major discoveries that will lead to products that will benefit the lives of all humankind. The state should be very proud that it has encouraged the biotech industry and the future of genomics, proteomics, and the new genetic medicine." **iQ**